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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,334	03/07/2007	Francesco Santangelo	U 016325-6	9753

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,334	SANTANGELO, FRANCESCO	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-16-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Preliminary Amendment filed June 16, 2006 is acknowledged. Claims 1-8 are presented and represent all of the claims under consideration.

A new Abstract is noted.

An Information Disclosure Statement filed June 16, 2006 is further acknowledged and has been reviewed to the extent each reference is presented in the English language.

Applicant is requested to send a complete list of his co-pending and related applications drawn to the administration of cystine and/or cysteine.

The abstract of the disclosure is objected to because there are presently no methods "for the preparation of oral medicinal products" under consideration. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to for the following informalities: The term "hemodialysis" is spelled incorrectly in claims 1, 2, 5 and 6.

Appropriate correction is required.

Claims 1 and 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1 and 5 lack clarity. Claim 1 is drawn to a method for preventing or treating oxidative stress resulting from hemodialysis treatment in patients suffering from chronic kidney failure. Claim 1 also appears to be drawn to a method for the treatment and prevention of acute or chronic kidney diseases. Claim 1 also appears to be drawn to a method for the treatment and prevention of End-Stage Renal Disease.

Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The instant claims are drawn to oxidative stress resulting from hemodialysis treatment in patients suffering from chronic kidney failure; to acute or chronic kidney diseases; and to end-stage renal disease, all in methods of treatment or prevention. There is insufficient written description for these claim limitations in the disclosure.

> M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

The claims encompass a plethora of possible conditions and pathologies of distinct etiologies. The specification fails to describe the administration of cystine, cysteine or mixtures thereof for use in any treatment modality.

To provide adequate written description of a claimed genus, such as renal diseases, the specification must provide sufficient distinguishing and identifying characteristics of the genus. In the instant case, only a broad general statement of "administration of cystine and/or cysteine for the prevention and treatment of oxidative stress resulting from hemodialysis in patient suffering from chronic renal failure" is provided on page 3 of the specification. There is no description drawn to any methods wherein a specific therapeutic endpoint is achieved.

Accordingly, it is not clear Applicant was in possession of the **full scope** of the claimed method at the time the invention was made. Adequate description requires more than a mere statement that treating oxidative stress resulting from hemodialysis, treating patients suffering from chronic kidney failure, treating acute or chronic kidney diseases and treating end-stage renal disease are part of the invention. The skilled artisan could not "immediately envisage" the claimed methods based on the description provided in the disclosure.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to the prevention or treatment of any acute or chronic kidney disease comprising administering cystine, cysteine or mixtures

thereof. The specification does not reasonably provide enablement for methods of prevention within the full scope of the claims.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir.1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547, the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is drawn to the prevention or treatment of oxidative stress resulting from hemodialysis treatment in patients suffering from chronic kidney failure, to acute or chronic kidney diseases and to end-stage renal disease. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of nephrology.

However, that factor is outweighed by the unpredictable nature of the various pathologies that are encompassed in the recitation "chronic kidney failure" and "acute or chronic kidney diseases." In cases involving unpredictable factors, such as the instant claim drawn to physiological activity, the scope of enablement varies inversely with the degree of unpredictability of the factors involved. One skilled in the chemical or biological arts cannot always reasonably predict how different chemical compounds might behave under varying circumstances. See *Ex parte Sudilovsky* 21 USPQ2d 1701.

On page 3 of the specification, only a broad general statement of "administration of cystine and/or cysteine for the prevention and treatment of oxidative stress resulting from hemodialysis in patient suffering from chronic renal failure" is provided. This mere statement does not provide support for preventing any acute or chronic disease and is not commensurate in scope with the instant claims. As evidenced by Applicant's submission on June 16, 2006 from The Merck Manual, chronic renal failure results from numerous causes. Therefore, the outcome of a particular therapeutic regimen is unpredictable.

The present disclosure is clearly not predictable for prevention of any disorder.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples drawn to a prevention modality in which cystine or cysteine is shown to be clinically effective for prevention of any renal disease. No guidance is provided drawn specifically to methods of prevention, as defined by the instant claims. Such an assertion is beyond the scope of the instantly claimed invention. The term "prevention" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases suffered by mankind cannot be totally prevented with current therapies.

The quantity of experimentation necessary

No direction is provided to distinguish therapy among the various disease states that are encompassed in the recitation "acute or chronic kidney disease." Absent

reasonable *a priori* expectations of success for using the claimed amino acids, one skilled in the art would have to test extensively many conditions to discover which exhibit an effect in a treatment or prevention modality. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Prevention entails the complete and absolute inhibition of the onset of any renal disease and any manifestation of the disease entirely.

Due to the known unpredictability of the art, and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that any acute or chronic kidney disease could be prevented following the administration of cystine or cysteine. Accordingly, the instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al., U.S. Patent 4,794,124.

Yamamoto teaches the oral administration of cysteine in amounts of 10-5000 mg to treat diabetic nephropathy, i.e., any pathology of the kidney. According to Applicant's submission, the citation The Merck Manual, page 1845, the most common cause of end-stage renal disease is diabetic nephropathy. The determination of whether to proceed with hemodialysis is based *inter alia* on laboratory determinations. Yamamoto fails to teach oxidative stress resulting from hemodialysis in patients suffering from chronic kidney disease.

However, Dall'Aglio teaches the administration of cysteine as a detoxicating agent to treat oxidative stresses. See page 1, where cysteine is stated to possess the same activity as α-lipoic acid for free radical reduction. Dall'Aglio teaches "oxidative stress" to mean any physiological and/or pathological condition characterized by an increase in the production of peroxides and free radicals in general, such as in the case of diabetes. See page 2, lines 2-6 and 9.

Therefore, in view of the combined teachings of Yamamoto and Dall'Aglio, one skilled in the nephrology art would have been motivated to administer cysteine to treat the oxidative stress resulting from hemodialysis treatment in patients suffering from chronic kidney failure with a reasonable expectation of success. Such would have been obvious because patients suffering from chronic renal failure with concomitant metabolic or circulatory decompensation conventionally require hemodialysis. Yamamoto teaches the oral administration of cysteine to treat diabetic nephropathy. Dell'Aglio teaches the administration of cysteine to treat oxidative stress in diabetics.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Yamamoto et al., U.S. Patent 4,794,124.

Yamamoto teaches pharmaceutical compositions for oral administration comprising cysteine. See column 2, lines 45-68. Intended use confers no patentable weight to composition claims. See **In re Hack**, 114 USPQ 161 (CCPA 1957).

No claim is allowed.

Zaloga et al., U.S. Patent 6,060,446, is cited to show further the state of the art with respect to the oral administration of cysteine to treat acute renal failure. See claim 6, column 8.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel, may be reached on 591-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 26, 2008

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614